# 13

# *Malaria*

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Malaria is a collective name for different diseases that may result from infection by any parasites of the genus *Plasmodium*. Four species of malaria parasites naturally infect humans: *Plasmodium falciparum*, *P. vivax*, *P. malariae*, and *P. ovale*. The characteristics of the disease vary with the intensity of the infection, the host's level of immunity, the adequacy of and opportunity for treatment, and the parasite's susceptibility to it.

Transmission between humans occurs through the bites of certain species of mosquitoes of the genus *Anopheles*. In this cycle, the parasite matures and reproduces sexually in the anopheline mosquito (the vector), which is therefore, strictly speaking, the parasite's definitive host, and human beings are its intermediate host.

## A Natural History: Parasite and Vector

The life cycle of the parasite follows a general pattern. The infecting parasite, an actively motile form called a sporozoite, is inoculated into the blood with the saliva of the biting mosquito. After about half an hour, the sporozoites invade liver tissue cells, where they develop and multiply. Small parasite forms called merozoites, capable of invading the red blood cells, burst into the blood—as many as 20,000 per successful sporozoite. The time needed to multiply in the liver, the pre-erythrocytic stage, varies with the parasite species: six to seven days for *P. falciparum*, fourteen to sixteen days for *P. malariae*, and seven to eight days for *P. vivax*, although some *P. vivax* parasites remain dormant in the liver for months, even a few years, in a form called hypnozoite. Once the parasites invade the red blood cells they initiate the cycle of development and multiplication that causes clinical manifestations of the disease. Disease symptoms are caused only by parasites in the blood. The late development of hypnozoites, therefore, gives the disease a long incubation period, or a pattern of cure alternating with repeated relapses, because common antimalarial drugs that may clear the blood of parasites are not effective against parasites in the liver. Merozoites invade red blood cells, where they grow and multiply to produce eight to twenty-four merozoites (depending on the parasite species), which rapidly invade new red blood cells. This development is accomplished in forty-eight hours for the so-called tertian malarias (benign, if from *P. vivax* and *P. ovale*; malignant, if from *P. falciparum*) and seventy-two hours for the quartan (from *P. malariae*). This development takes place in the peripheral blood for *P. vivax*, *P. malariae*, and *P. ovale*. But with *P. falciparum*, only red blood cells infected with very young parasites (called ring forms) are found in the peripheral blood; those infected with developing or dividing parasites are sequestered in the capillaries of such internal organs as the brain and cause the severe manifestations typical of *P. falciparum*.

Some parasites do not follow the cycle of asexual reproduction just described. Instead, they differentiate into male and female gametocytes, which are eventually taken up by an *Anopheles* mosquito. In the mosquito they can mature, achieve fertilization, and multiply in the stomach wall, producing about 1,000 sporozoites, which burst into the mosquito's body cavity and finally invade the salivary glands. This sexual cycle takes between nine and thirty days or more, depending on the temperature and the parasite species.

Not all species of anophelines are vectors of malaria, and those that are vary greatly in their ability to transmit the disease. General or specific refractoriness may be due to many causes, for example, because the plasmodia is unable to develop or to invade the salivary glands, or because the mosquito cannot live long enough to complete the parasite's extrinsic cycle, or because the mosquito has so little contact with humans (for example, is so unlikely to bite humans) that it is unlikely to bite a human after becoming infected. Of the roughly 400 species of *Anopheles*, only about 60 are vectors of malaria under natural conditions; some 30 of these are of prime importance.

As for all mosquitoes, the habitat of the immature *Anopheles* is water. Eggs are all laid on or on the edge of water and hatch in two to three days to produce larvae (wrigglers). Larvae develop through five aquatic stages—four larval and one pupal—to produce adult flying mosquitoes. Only the female mosquito bites; it does so because it needs blood for its eggs to mature. The male feeds on vegetable juices. Mating occurs only once, soon after the adult female emerges. The female stores the spermatozoa in a deposit called a spermatheca. The aquatic stages commonly last seven to twenty days, depending on the temperature. The adult female may live from a few days

to well over a month, going through several cycles of blood feeds and egg laying (some 100 to 200 per batch), every two to four days. Survival and egg development depend mainly on temperature and relative humidity. In extreme climates mosquitoes may go into hibernation, which allows some of them to survive the winter in temperate climates.

Depending on the species, larval habitats vary enormously, reflecting mosquitoes' evolutionary adaptability. The habitats range from permanent to transient bodies of water; from fresh to brackish water; from standing water to flowing canals and open streams; from water in open sun to that in deep shade; from shallow pools to deep wells; from clean drinking water to water highly polluted with organic matter; from large open marshes to the tiny pools of water that collect between the leaves of bromeliads in plant axils, trees, rocks, crab holes, cattle footprints, or discarded artificial containers. But the characteristics of breeding places are rather narrowly defined for each species, so larval habitats can be modified for control of mosquito species.

The seasonal availability of breeding places and the great influence of weather conditions on mosquito activity and survival are largely responsible for the marked seasonality in mosquito population densities and malaria transmission in most areas outside of permanently humid tropical areas.

Specific behavioral characteristics of mosquitoes may also affect their vectorial ability. Mosquitoes' preferences for feeding on humans or animals and their frequency of feeding are important determinants of the probability of their transmitting malaria. Human dwellings and domestic animal shelters—particularly those with thatched roofs, dark corners, and many cracks in the walls—are good resting places in which mosquitoes can digest the blood they have consumed while their eggs mature. Such buildings favor mosquito survival but are also vulnerable to insecticidal spraying.

## Malaria as a Disease

The chief symptom of malaria is fever, periodic bouts of which tend to alternate with days of less or no fever. The classical paroxysm of fever lasts eight to twelve hours, typically in three stages: cold shivering rigor, burning dry skin, and drenching sweat that lowers the temperature. This pattern is more typical of *P. vivax* (tertian periodicity) and *P. malariae* (quartan) than of *P. falciparum*, which typically involves prostrating fever, with brief and incomplete remissions, more often irregular than clearly periodic. Untreated, the acute attack is shorter than that of *P. vivax*; in fatal cases, death often occurs in two to three weeks and sometimes as soon as two to three days after the onset of symptoms. Repeated infections give rise to an immune response in the host which eventually controls the infection and the disease. Untreated or incompletely treated infections will produce several recrudescences, after long symptomless periods, from parasites surviving in the blood. By this mechanism alone, *P. falciparum* may persist for one or two years, whereas *P. malariae* has been reported to recrudesce up to fifty-two years after last exposure to infection. With *P. vivax*, true relapses may occur, because latent hypnozoites will mature in the liver and invade the blood after other parasites have been completely eliminated from it. Without reinfection, *P. vivax* may persist for three to four years.

In the absence of other complicating factors, acute severity and mortality occur almost exclusively in *P. falciparum* infections. This parasite causes the surface of infected red blood cells to become adhesive and to be sequestered in the capillaries of internal organs, leading to the pathological changes responsible for cerebral malaria and the serious renal, hepatic, and gastrointestinal dysfunctions. Other severe complications such as shock, pulmonary edema, severe anemia and hemoglobinuria (or blackwater fever), are the results of more complex mechanisms.

*P. falciparum* malaria can lead rapidly to death, so it is important to recognize signs of severity early and refer the patient immediately for medical care. These signs include shock, anemia, convulsions, jaundice, hyperpyrexia, renal failure, impaired consciousness, spontaneous bleeding, macroscopic hemoglobinuria, and pulmonary edema or respiratory distress. Health services that suspect severe malaria should treat it as a medical emergency, providing immediate treatment and, whenever possible, laboratory monitoring of such signs of severity as hypoglycemia, parasite density, and an imbalance of fluids and electrolytes.

The risk of severe malaria is almost exclusively limited to those who are not immune. In highly endemic areas this risk affects children older than three to six months, who have lost the immunity transferred from their mother, up to the age of about five years, when surviving children have developed their own immunity. African health authorities report that in the last few years cerebral malaria is being seen increasingly often in older children and young adults. It has been suggested that this may be the result of urbanization and personal protection, which reduce the risk of infection and delay the development of immunity. Severity in adults is seen in areas of low endemicity, where people may reach adulthood without immunity. Equally at risk are immigrants and travelers from nonendemic areas—particularly laborers, who are often concentrated in camps, where nonimmunes and the infected live side by side in overcrowded conditions where the risk of transmission is high. Also at risk are pregnant women, possibly because natural immunity is depressed during pregnancy.

Most deaths from malaria occur in young children living in highly endemic areas of tropical Africa and the western Pacific islands. The most common causes of death are cerebral malaria and severe anemia. Malaria may also contribute seriously to the severity of other childhood diseases.

In pregnancy, *P. falciparum* malaria in the nonimmune may lead to death, abortion, premature delivery, or low birth weight. In the semi-immune inhabitants of highly endemic areas, malaria represents a serious risk in a first and second pregnancy. Pregnant women are more easily infected (and are susceptible to anemia, hypoglycemia, and other complications) because the placenta is a preferential site for parasite development. Malaria is an important cause of low birth

weight and high neonatal mortality in first- and second-born children in endemic areas. It has been suggested that the build up of a total uterine immune response may account for the disappearance of these effects on subsequent pregnancies (McGregor 1982).

## The Public Health Significance of Malaria

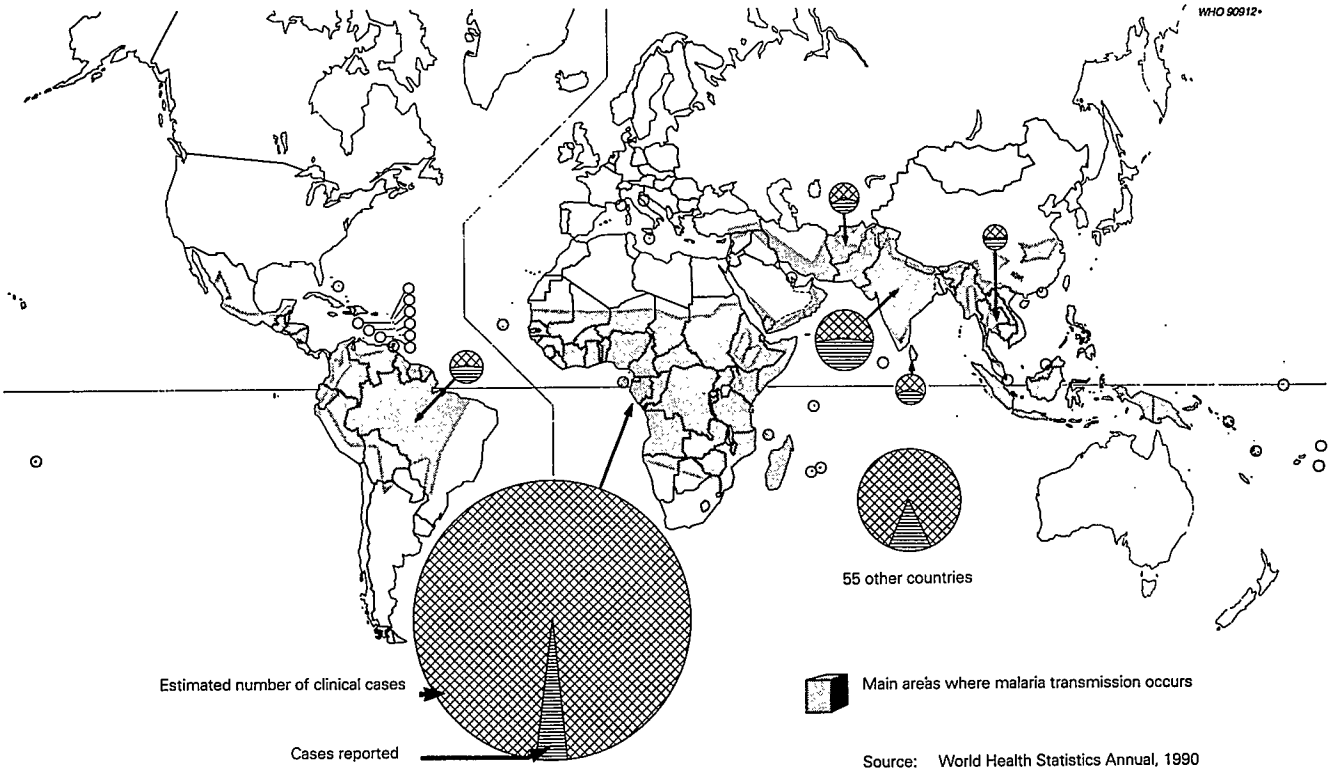
Roughly 110 million clinical cases of malaria develop annually. Some 270 million people are infected, carrying malaria parasites, although not necessarily developing symptoms. Indigenous malaria still exists in some 100 countries or areas. Accurate estimates are impossible because the accuracy of reporting varies considerably. Reporting from tropical Africa—where more than 80 percent of the clinical cases and 90 percent of the parasite carriers may be found—is especially irregular and fragmentary. Reported cases are believed to represent about 2 to 20 percent of the actual cases.

### *Geographical Distribution*

Every year, in the *World Health Statistics Quarterly*, the World Health Organization (WHO) publishes an overview of the world malaria situation (map 13-1). The overview for 1990 (WHO 1992) indicates that the world population (about 5,300 million people) can be classified according to people's experience with malaria and their place of residence as follows:

- Areas in which malaria never existed or disappeared without specific antimalarial interventions: 1,431 million people, or 27 percent of the world's population.
- Areas in which endemic malaria disappeared after a specific campaign to control it was implemented and the area has remained malaria-free: 1,696 million people, or 32 percent of the world's population.
- Areas in which endemic malaria was reduced or even eliminated after control measures were implemented, but the disease was reinstated and the situation is unstable or deteriorating: 1,700 million people, or 32 percent of the world's population. This category includes zones (which include about 1 percent of the world's population) in which the most severe resurgence of malaria has recently developed as a result of significant ecological or social changes, such as sociopolitical unrest and agricultural or other exploitation of jungle areas.
- Areas in which endemic malaria remains basically unchanged and no national antimalaria program was ever implemented, because of the enormous difficulties of

***Map 13-1. Malaria Incidence***




*Note*: The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.
*Source*: Reproduced by permission of the World Health Organization, Geneva from *Weekly Epidemiological Record* 67 (22–23): 162–167/169–174 (1992).

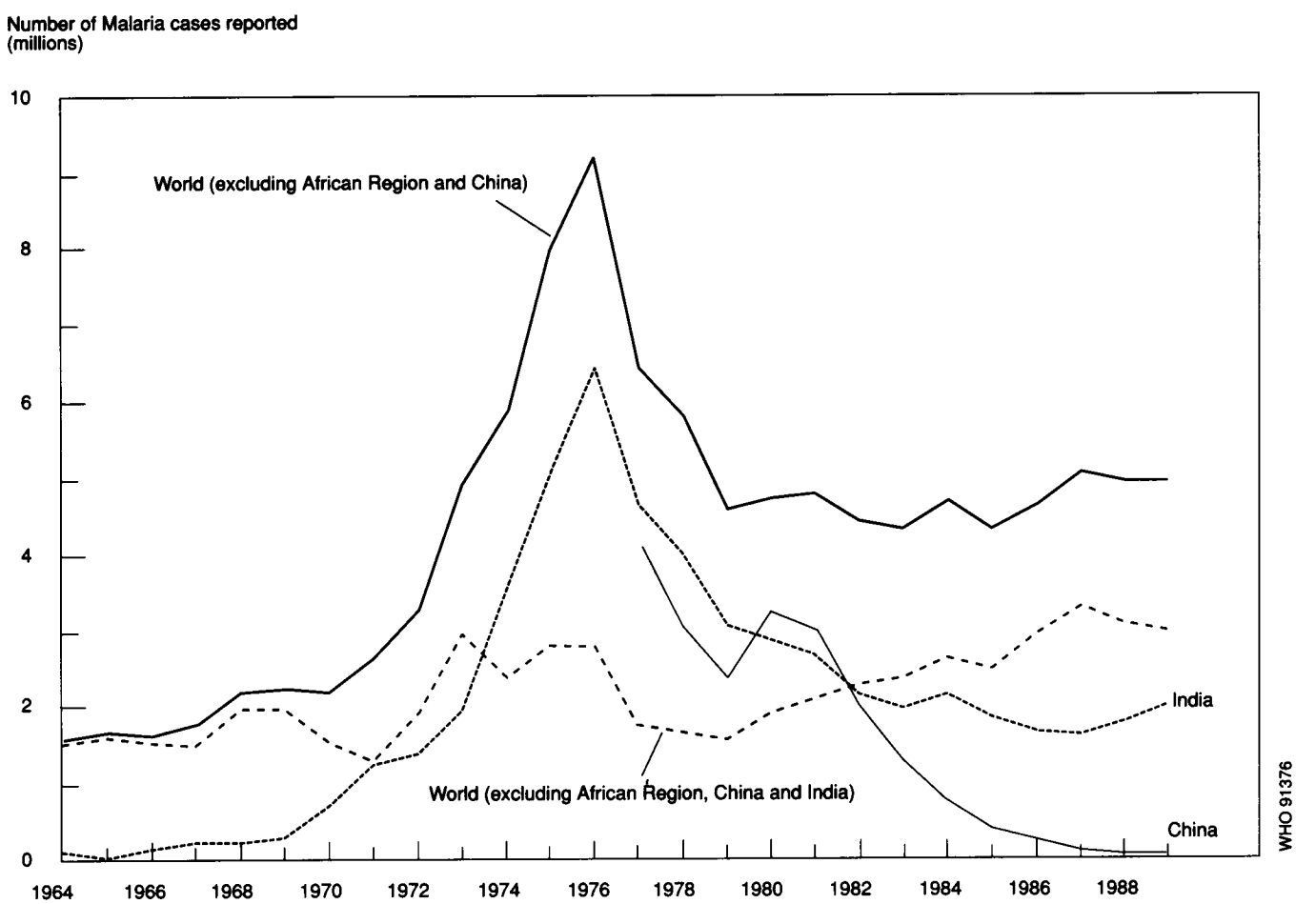
achieving control: 500 million people, or 9 percent of the world's population. Malaria is most endemic in these areas, which contain 85 percent or more of the malaria cases in the world. These areas are mainly in tropical Africa; in some of them—including forested and medium-altitude areas—pilot projects were reportedly successful in interrupting malaria transmission, but in low savanna areas, particularly in the Sahel, no pilot projects ever reported full success.

### *Trends*

The evolution of the malaria problem is traditionally described by the number of registered cases reported to WHO by member states. Figure 13-1, which excludes information on Africa because of inadequate, irregular reporting from that continent, shows the effect of the massive resurgence of malaria transmission in India in 1976 and its subsequent control. Changes in China are shown separately, because the Chinese started officially reporting to WHO only in 1977. China did not implement a national malaria control program until it had developed a health infrastructure that has been considered a precursor of primary health care; the pattern of malaria incidence is similar to the pattern in countries that eradicated malaria (map 13-1). If India and China are not taken into account, the incidence of malaria in the world did not show a clear trend until the late 1970s, when it started a slow but steady deterioration. Data from India indicate that, after recovery from the 1976 epidemic, improvement slowed down and the situation seems to be stagnating.

The general pattern described here masks great local differences, not only in the intensity of the problem, but also in the pattern of its evolution over time. The geographical distribution of malaria is far from uniform; it can be seen that malaria clearly thrives in certain areas, and it may be said that it occupies definable socioecological niches. The limits of malaria foci are much more diffused than those for contagious diseases such as smallpox, however, so it is more difficult to target their control.

***Figure 13-1. Number of Malaria Cases Reported, 1964–89***




*Source:* WHO 1991.

### *Morbidity in Tropical Africa*

In the last decade African countries south of the Sahara have reported between 2 and 20 million cases a year to WHO; but extrapolating from fever and parasite surveys, it is estimated that 100 million clinical malaria cases may occur every year, and 275 million persons may carry the malaria parasite. The levels of endemic malaria are among the highest in the world. Extensive forest or savanna areas up to about 1,000 meters high, with rainfall of more than 2,000 millimeters a year, are classified as holoendemic. Areas between 1,000 and 1,500 meters high or lowland areas with 1,000 to 2,000 millimeters per year of rainfall are characterized as hyperendemic. As altitude increases above 1,500 meters or rainfall decreases below 1,000 millimeters per year, malaria becomes less endemic, concentrating in progressively smaller valleys or where favorable microclimatic conditions and mosquito-breeding places exist or are created by such human activities as irrigation, dam construction, and the establishment of fish ponds. Of course, altitude and rainfall are only rough indicators of malaria's endemicity; other factors, such as temperature, humidity, the distribution of rains, and the slope and permeability of the soil, also play important roles.

As endemicity decreases, the potential for epidemic outbreaks increases because fewer people have a chance to develop immunity. Equally, in areas of marked seasonality, as in the dry savanna of the Sahel, the transmission season, even if it occurs every year, takes on the characteristics of seasonal epidemics, at least as it affects younger age groups. Severe, large-scale epidemics occur in areas that have been free from transmission for several years in a row, and they exhibit a secular periodicity determined by the semicyclic occurrence of prolonged heavy rains or other climatological determinants. Such epidemics have been historically reported in high-altitude areas following abnormally warm and rainy summers. Such was the dramatic epidemic in the highlands of Ethiopia in 1958, which caused more than 3 million cases and claimed an estimated 150,000 deaths. They also occur in dry areas after abnormally heavy and prolonged rains, as in the epidemic of 1975 in Gezira and Central Sudan and the 1988 epidemic in Khartoum and Northern and Eastern Sudan. In 1988–90 a number of epidemics, or serious exacerbations of endemicity, occurred in several highland areas of Africa, particularly in Botswana, Madagascar, Rwanda, Swaziland, and Zambia.

In the high plateau of central Madagascar increasingly extensive and severe epidemics occurred between 1986 and 1988, reaching dramatic proportions in the first four months of 1988, when tens of thousands of people died. One of the main causes of this series of epidemics was that the DDT spraying campaign of the 1960s and early 1970s seems to have eliminated the main vectors of malaria *A. funestus* and *A. gambiae sensu stricto* so that malaria transmission was interrupted for about twenty years. But after spraying was discontinued and because of other opportunistic circumstances, both species progressively spread in the high plateau.

Smaller and more localized malaria epidemics have occurred when colonization efforts or agricultural or other economic development projects in endemic areas have attracted nonimmune populations from nonmalarious areas. This happened in the late 1950s, for example, when the lowlands of Kigezi (Uganda) began to be colonized by people from the overpopulated highlands, resulting in a tragic malaria epidemic with extremely high mortality. This led to the establishment in 1959 of one of the few successful malaria eradication pilot projects in Africa (de Zulueta and others 1961). In the last few years malaria endemicity has reportedly spread in the highlands of Amani in Tanzania. This increased transmission has been attributed to the active colonization of those areas and the subsequent intensification of agriculture and the attendant terracing and leveling of the land in and around human settlements, which increased potential anopheline breeding places (Matola, White, and Magayuka 1987).

Another possible factor in the apparent increase in epidemic potential in the last few years in the highland areas in Africa is the so-called greenhouse effect, by which the accumulation of carbon dioxide and other gases in the atmosphere may retain heat. In Madagascar the average temperature in the coastal areas was 0.5 degree centigrade warmer than in the previous thirty years; in the high plateau the difference was about 1 degree centigrade. These figures may not be fully comparable because data for the high plateau may be influenced by local ecological changes, such as the growth of Antananarivo. Still, an increase of even 0.5 degree centigrade could increase the potential transmission period in marginal areas, which might change a normally nonmalarious area into one subject to seasonal epidemics (de Zulueta 1988).

### *Morbidity in Other Malarious Areas*

Outside tropical Africa, most malarious countries have similar reporting systems that permit some degree of comparison. As for the intensity of the problem, about 80 percent of the 5.01 million cases reported to WHO in 1990 (not including tropical Africa) are concentrated in eleven countries. They are, in decreasing order of total number of reported cases, India, Brazil, Afghanistan, Sri Lanka, Thailand, Indonesia, Viet Nam, Cambodia, China, Solomon Islands, and Papua New Guinea. These countries represent 65 percent of the population living in the world's malarious areas, excluding tropical Africa. India and Brazil, with only 26 percent of the population, report 46 percent of the cases. With only 34 percent of the population, the first seven countries report 70 percent of the cases. And within these countries, malaria is focused in certain areas. In India, for example, six states (Orissa, Uttar Pradesh, Punjab, Madhya Pradesh, Gujarat, and Assam) have 66 percent of the cases. In Brazil, 97 percent of the cases are in Amazonia, which has only 15 percent of the country's population; two states (Rondônia and Pará) report 70 percent of the cases, and four municipalities in Rondônia and four in Pará report more than 60 percent of the cases in those states.

These countries and areas show great variability not only in the intensity of the problem but also in its evolution in time. Cases reported annually to WHO since the mid-1960s show distinct patterns:

- Malaria declined and the situation has remained favorable in Algeria, China, Costa Rica, Cuba, Egypt, Korea, peninsular Malaysia, Morocco, Panama, Paraguay, and Tunisia.
- Malaria increased markedly in certain areas in Afghanistan, Bangladesh, Belize, Bhutan, Bolivia, Brazil, Cambodia, Colombia, French Guiana, Guatemala, Guyana, Madagascar, Mexico, Myanmar, Nepal, Papua New Guinea, Peru, the Philippines, Saudi Arabia, Solomon Islands, Thailand, Vanuatu, and Viet Nam.
- The incidence of malaria has oscillated—at relatively short cycles and with a quasihorizontal general trend, at least since the early 1960s—in Argentina, El Salvador, Honduras, Indonesia (the outer islands, reporting since 1970), Iran, Malaysia (Sabah), Nicaragua, Surinam, and the Republic of Yemen.
- In the last twenty years, one or two relatively short but significant resurgences, followed by renewed control, have occurred in the Dominican Republic, Ecuador, Haiti, India, Indonesia (Java and Bali), Iraq, Libya, Malaysia (Sarawak), Mauritius, Oman, Pakistan, Somalia, Sri Lanka, Syria, Turkey, Venezuela, and Yemen.

The only purpose of this preliminary classification is to stimulate analysis of the patterns of change. Groupings are based on total numbers of reported cases, and the fact that two countries appear in the same group does not indicate similarities in other epidemiological characteristics.

Except for India and China (which are significant producers of cases because of their great size) and Sri Lanka (which may be changing from a pattern of periodic resurgence because of sociopolitical unrest), most large producers of cases are in the second group. These countries are characterized by recent efforts to increase the exploitation of natural resources (through agricultural colonization of forest or jungle areas) or by civil war or sociopolitical conflict (including illegal drug trade) and large movements of refugees or other mass migrations. Eight of the eleven main producers of cases have been on that list since at least 1986.

All the countries in the first group, where malaria has declined, have shared a degree of social stability and socioeconomic development, including health services accessible to the public. The countries in the third group have suffered periodic bouts of malaria, followed by remobilized control efforts, after which the situation improved but could not be maintained, so malaria recurred. This pattern of "fire fighting" may progressively improve matters in the more developed areas as people become less tolerant of epidemics and health services become more responsive. In marginal areas, the response is nearly always late and possibly ineffective, because it often comes when the epidemic is naturally declining.

### *Drug Resistance and Proportion of* P. falciparum

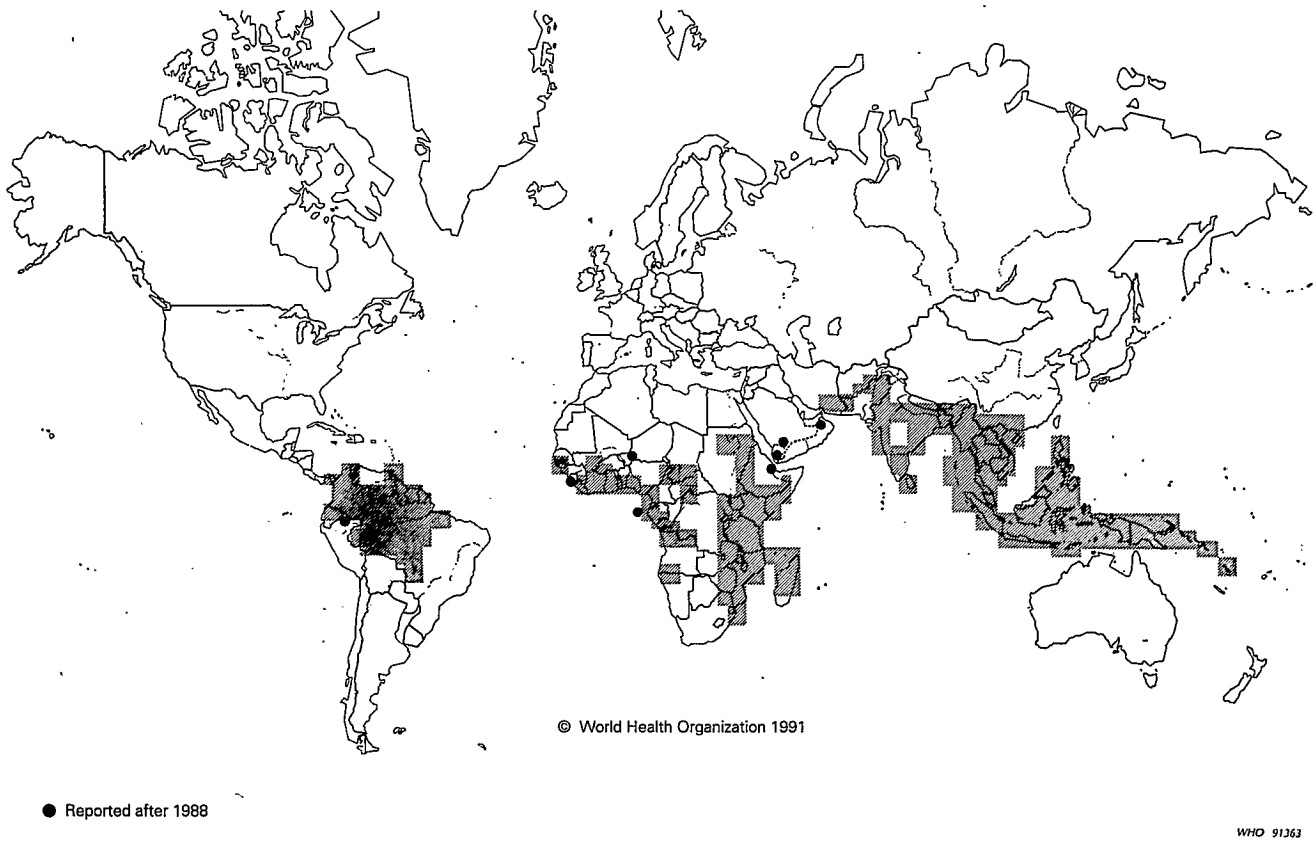
The proportion of *P. falciparum* in endemic areas outside tropical Africa, where *P. falciparum* remains the predominant species, was 38 percent in 1990 (compared with 15 percent in the early 1970s). In the last few years there has been an increased selection and progressive dispersal of *P. falciparum* parasites resistant to antimalarial drugs, because these drugs are used increasingly as prophylactics and for self-medication, usually in insufficient doses (see map 13-2). The problem of drug resistance has been particularly alarming in Africa; in recent years it has spread across the continent and is now developing rapidly in West African countries. Its continual intensification hampers efforts to provide adequate treatment in rural areas. It is difficult to assess how much to attribute this phenomenon to the migration of resistant parasites and how much to local selection, because both mobility and drug consumption have increased considerably. For some time the widespread use of chloroquine was advocated as the most effective way to reduce deaths from malaria in Africa; chloroquine, it was said, should be treated as a commodity and not as a drug. In many places in Africa people use chloroquine more often than aspirin for minor fevers and aches. Chloroquine has, no doubt, helped reduce deaths from malaria, but maintaining this gain will require targeting antimalarial drugs to those actually suffering from malaria, particularly in areas where resistant parasites require the use of more toxic and less affordable drugs.

### *Mortality*

Most deaths from malaria occur in tropical Africa. As in all highly endemic areas, deaths occur most among the young. Maternal immunity transmitted to infants may reduce mortality in the first three to six months of life, but this effect may be masked in areas of marked seasonality. Past studies indicated mortality rates between ten and thirty per thousand in infants and between about seven and eleven per thousand in children one to four years old. In 1962 the WHO Regional Office for Africa estimated that every year between 200,000 and 500,000 African children die from malaria (Pampana 1969). In 1969, Bruce-Chwatt put that figure at about 1 million, a figure extensively quoted ever since. Molineaux (1985), reviewing the effect on infant mortality of some malaria control projects, especially in Kisumu (Kenya) and Garki (Nigeria), concluded that malaria was responsible for about 20 to 30 percent of infant deaths. Greenwood and others (1987), studying deaths from malaria in the Gambia, concluded that the mortality rate from malaria was 6.3 per 1,000 for infants and 10.7 per 1,000 for children one to four years old, representing 10 percent of the deaths of children less than a year old and 25 percent of deaths for children one to four.

There are signs that in some parts of Africa general infant and malaria-specific mortality may be declining, often independently of specific interventions, reflecting social develop-

***Map 13-2. Areas where Chloroquine-Resistant* Plasmodium Falciparum *has been Reported***

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ment and general education. Studies in the Congo and Burkina Faso in the late 1970s indicated that malaria-specific mortality might be lower than expected in areas where, some decades ago, malaria was a significant cause of infant mortality. The authors (Vaise and others 1981) attributed their findings to the widespread, albeit indiscriminate, use of antimalarial drugs. Often these drugs were used in doses inadequate to eliminate parasites but effective enough to produce a clinical cure and prevent death, even if collectively such use could be contributing to the selection of drug-resistant parasites. The wide availability of antimalarial and other active drugs has also been identified as possibly contributing to the general decline in infant mortality observed in the Kisumu area of Kenya. There, between 1972 and 1976, infant mortality reportedly declined from 157 per 1,000 to 93 per 1,000 during an effective malaria control program (spraying fenitrothion inside houses). Between 1981 and 1983, a decline in postneonatal mortality (from 73 to 67 per 1,000) and a marked drop in the mortality of children of one to four years (from 25 to 18 per 1,000) were recorded after implementation of a program of community-based antimalaria treatment. But most of that decline was attributed to a measles epidemic in 1981–82; malaria-specific mortality, being relatively low, did not change significantly in the year of intervention. This study (Spencer and others 1987) confirmed in a small rural area the general observation that differences in child mortality can be explained largely by differences in maternal education, which no doubt influences the amount of drug use but, more important, improves hygiene and general living standards. Differences in infant mortality between districts in Kenya, as reported in the 1979 census, ranged from 38 to 153 per 1,000. When spraying in Kisumu ended, in 1976, the area did not return to the previous infant mortality rates. Infant mortality rates for the district in which this area is located declined from 220 in 1959 to 181 in 1969 and to 147 in 1979 (Spencer and others 1987).

Deaths from malaria outside tropical Africa occur mainly among nonimmunes who become infected by *P. falciparum* and get sick where appropriate diagnosis and treatment are unavailable. This happens especially to newcomers to endemic areas, such as agricultural workers, laborers, gold and gem miners, and prospectors in recently colonized or other frontier areas of economic development. Most affected are young adults, although whole families of settlers may be affected—for example, in the tropical jungles of South America (especially

the basins of the Amazon and the Orinoco), in the outer islands of Indonesia, Sabah, Kalimantan, and, on a smaller scale, throughout the tropics. In the Brazilian Amazon, an estimated 6,000 to 10,000 people a year die from malaria (J. Fiusa Lima, personal communication, 1990).

### *Possible Patterns of Morbidity and Mortality: 2000, 2015*

Malaria transmission is focal and depends on the dynamics between humans and the vector, parasite, and environment. More important, it depends on the effectiveness of control efforts, socioeconomic development, and political stability. It is thus quite risky to generalize about future patterns of morbidity and mortality. Given the increasing resistance of the parasite to antimalarial drugs, however, treatment of malaria in the future will be more difficult and less effective, thereby increasing the risk of both morbidity and mortality. Although new drugs are being investigated, and work is progressing on various potential malaria vaccines, alternative first- or second-line drugs or a vaccine are, even under optimistic circumstances, several years away.

Furthermore, population instability in areas in which there is the potential for malaria transmission is usually associated with an increasing burden of illness, including mortality due to malaria. This instability might result from political conflicts, economic development or relocation schemes, migration because of population pressure, or natural disasters. Examples from Brazil, Thailand, Indonesia, and Sri Lanka may illustrate different facets of this problem. To the extent that development projects ignore effects on health or that political conflicts create large refugee populations, malaria is likely to increase in each such local situation. Conversely, adequate socioeconomic development and political stability will facilitate effective and sustainable malaria control.

As to patterns of morbidity and mortality in the future, it is safe to predict that there will be more morbidity and possibly mortality as a result of malaria in several areas, but how much more and, more specifically, which regions will bear most of the burden, is less obvious. Well-documented case studies could serve as examples of potentially devastating effects, given similar scenarios in other areas of the world (that is, Brazil, Madagascar, Sudan, Indonesia, Afghanistan, Sri Lanka, and so on).

But most important in view of the presently deteriorating worldwide malaria situation referred to earlier, a forceful effort to rehabilitate, activate, or develop new malaria control activities in those countries most affected is crucial. Without such an effort malaria patterns in the year 2000 will be entirely different and substantively worse than the ones predicted.

### *Economic Costs of Malaria*

The economic costs of malaria theoretically would include its effect on the economy and economic development, on the local community, on the household, and on the individual. There have been few community-based methods used to evaluate the economic effect of malaria. The study by Conly (1975) highlights the problems encountered in attempting to quantify the effect on economic development resulting from the difficulty of collecting and processing data on a sufficiently large population and the complexity of the interactions of the parameters measured.

COSTS OF MORTALITY AND MORBIDITY. The costs that malaria imposes are borne through increased mortality and through high morbidity rates. The effect of mortality will vary with the age distribution of deaths, which in turn vary by ecological zones. In Africa, where most deaths are among infants and young children, the effect of and the perception of mortality will be different from other areas, where the deaths are among the main breadwinners or primary caretakers of families. Mortality and morbidity among adults are high in areas of low to moderate endemicity. See Over and others 1989 on the consequence of adult deaths.

MALARIA AND PRODUCTIVITY. Public health activities have been justified as improving productivity ever since debates about the "laziness disease" at the beginning of this century (Garcia 1981). Malaria is a classic example of a debilitating disease that impairs productivity. As the most prevalent disease in the poorest rural areas, malaria produces recurrent infections with attacks of fever in the warm and rainy seasons, when most workers are needed to collect crops. Often, affected people also suffer from malnutrition and other infections and lack of medical care. In areas subject to epidemics, these also tend to strike at times of peak demand for agricultural work.

The focus of much of the research has been on attempting to measure the effects of bouts of illness on lost output of workers. This research has been reviewed in Barlow and Grobar 1986. Research on the physical effect of the disease can be found in Conly 1975; Malik 1966; Russell and Menon 1942; and van Dine 1916. Days of disability per case of malaria estimated in these studies range from five to twenty. Other physical measures include effects on output or land cleared. Audibert (1984) sets values for the former varying from 0 to 1.5 for the elasticity of output of rice with respect to malaria prevalence, whereas Bhombore, Brooke Worth, and Nanjundiah (1952) found a reduction of 60 percent in cropped area in families with malaria. Conly (1975) traces a variety of adjustments in farm families in Paraguay, including increases in labor input per unit output as well as reallocations of land and hired labor. The reallocations of land entailed replacement of crops of high value whose crop season was malaria prone with crops of relatively low value whose crop season was not. De Castro (1985) finds that such reallocations may include an increase in the workload of healthy family members. Although this may be seen as an ameliorative factor which reduces the net effect of the disease, it may simply mean that some costs of the disease are borne by others besides those who are ill. In Southern Rhodesia it has been estimated that the

loss of manpower to malaria was 5 to 10 percent of the labor force, with the heaviest incidence at the peak of agricultural production.

Estimates are much lower in highly endemic areas, where anyone who survives childhood can generally tolerate a malaria infection, showing only minor symptoms at most, although malaria is an important contributing factor in severe anemia. Brohult and others (1981), in a study in Liberia, found no detectable loss of physical ability in people with malaria parasites in their blood, but they did find a marked correlation between anemia and loss of physical ability.

It is a common convention in the literature to use the parameter of seven days of work lost to disability per bout of malaria in assessing a program when the parameter is not independently estimated (see Niazi 1969; Quo 1959; San Pedro 1967/68; and Sinton 1938); when independently estimated, the parameter varied between five and fifteen days. A further issue, raised by Wernsdorfer and Wernsdorfer (1988), is the undermining of the effectiveness of investment in education. In highly endemic areas, where adults normally have acquired sufficient immunity to make the symptoms less severe, schoolchildren are more severely affected. Judging the degree of impairment caused by illness would be hard to do and one can only wonder at the cost. Macdonald (1950) estimated that the learning of 35 to 60 percent of children may be impaired by malaria.

Other studies emphasize direct financial benefits from activities made possible by eradication or control. These are also surveyed in Wernsdorfer and Wernsdorfer (1988). Malaria has hurt economic development projects as well as armies at war and police forces or border patrols in endemic areas. Malaria had to be overcome for the successful construction of the Panama Canal and most roads and railways in tropical countries, for the agricultural development of the Roman campagna and the Venezuelan llanos, for the building of railways and roads in tropical areas, and for the protection of armies from World War I through Viet Nam. Agricultural development and mining in tropical jungle areas, which attract workers from densely populated, often nonmalarious, areas, form one of the particular problems associated with malaria. An example of research into the benefits of malaria control in this situation is given by Griffith, Ramana and Mashaal (1971), who estimate the increased profits derived from allowing workers to enter new areas for mining. Forgone profits are the measure of the cost of disease. Sinton (1938) documents many cases in India where malarious regions prevented an expansion into new territories, resulting in substantial losses in forgone earnings. Demographic changes since then, however, have probably made such opportunities for expansion much rarer in the subcontinent.

DISTRIBUTION OF COST. Litsios (1990) highlights the uneven distribution of malaria risk across a population. Data from Adana, Turkey (Yumer 1980), for example, show that anopheline bites per person were five times more frequent in the tents of migrant workers than in the houses of village residents. Malaria has been concentrated among migrant laborers in most areas where there is extensive cultivation of cotton and sugar cane and in some areas where coffee, bananas, and rice are cultivated. Litsios (1990, p. 8) concludes that "as malaria becomes a problem to be primarily found in marginal or fringe areas, it becomes a problem that is identified with marginal people." This can be seen by the tendency in some countries to associate malaria with "foreigners" or minority migrant groups, who are then accused of being responsible for carrying the parasites into areas that might otherwise be malaria-free. In endemic areas the burden of malaria is also borne disproportionately by the poor.

PROBLEMS IN MEASURING COST. The focus on days lost from work or output forgone is oddly narrow. With regard to welfare, two alternative measures would be preferable. The first is the compensating variation in income, or, the amount one would be willing to pay to avoid having the disease altogether. The second is the equivalent variation, the willingness to accept, or the amount one would need to be paid to accept having the disease. In many contexts, these two measures are similar, but in cases in which possible mortality is involved the latter could generate much larger measures of costs than the former. Willingness to pay is bounded by ability to pay or lifetime earnings. In practical application, it would be limited by borrowing constraints as well. Willingness to accept is under no such limitation. Either of these measures would capture the subjective, even psychological effect of the disease. In any case, using a measure which respects personal preferences would be more inclusive than simply including the instrumental effects of the disease on the productive capacity of the worker. There are a number of objections to using these alternative concepts. They require defining which set of preferences (before or after falling ill) is relevant for the comparison. The most important criticism, though, is that obtaining this number requires a significant research effort. Such calculations have been made in the literature on environmental effects but are not widely used. It is possible to infer a lower bound, though, by calculating the total costs required to obtain treatment. The total costs borne by families and individuals include payments for treatment, time and transport costs in seeking treatment, time costs for family members who look after the patient, and time and money costs of preventive action taken by households and the community. These costs vary greatly with variables such as access to primary health care, national drug distribution policies, the presence of chloroquine resistance, the level of malaria endemicity, the behavior and bionomics of the local vector(s), and whether or not malaria is perceived as a serious health problem by the local community. There are two main sources of underestimation. First, this calculation misses costs before treatment is sought. Second, there are those (inherently hard to measure) who have decided that the costs of seeking treatment are too high in relation to the costs of letting the disease run its course. For them, there is still a relevant cost

and degree of necessary compensation. For people in remote areas, or those afflicted at peak agricultural seasons (when implicit wages are high, both for the person falling ill or, in the case of children especially, for those needing to accompany the person), or (more difficult to evaluate) those who are uninformed about treatment prospects, these costs can be high.

In their careful study of Thailand, Kaewsonthi and Harding (1986) attempted, among other things, to measure the costs borne by patients in seeking care. These were dubbed "external costs," that is, external to the malaria control organization. They amounted to $20 per positive case, or nine times the average wage. This estimate is for people presenting at the malaria clinic and therefore does not include those who have handled the disease in other ways. This study includes costs entailed in seeking local treatment before travel to the clinic. These amounted to 15 percent of the costs per positive case and are a component of the full cost to those who do not seek formal treatment. The degree of underestimation of the cost to sufferers is probably quite high. Time lost before and after seeking treatment can be considerable and varies with the quality (primarily speed) of service provided. This varies substantially within Thailand, let alone across countries.

Because the costs of malaria are borne disproportionately by the poor, there are further issues of aggregating individual costs into social costs. Whether disease averted should be weighted by the income of the sufferer, because of social welfare consideration or the possibility of successfully seeking treatment, is an ethical issue to be appraised by policymakers.

In summary, Andreano and Helminiak (1988, p. 35) state that "despite the many studies and the excellent work by Barlow and Conly, which represent methodological advances in the study of tropical diseases, we remain woefully ignorant of the social and economic effect of malaria in those countries of the world where it is prevalent." They also emphasize that findings in many of these studies cannot be easily generalized from one area to another.

## Malaria Control

The idea of eradicating malaria, postulated as early as 1916, gained currency after World War II. Malaria epidemics had devastated parts of southern Europe, and DDT had been extremely effective in controlling not only those epidemics but also endemic malaria in both temperate and tropical areas, including Venezuela, British Guiana, and Taiwan. The Expert Committee on Malaria of the newly created World Health Organization, in its first five reports, adopted a cautious attitude, expressing concern about increasing reports of technical problems and of some disappointing results in the use of DDT, particularly in Africa. But the goal of eradicating malaria became irresistible, and the impending resistance to DDT was seen as a reason for racing to eradicate malaria before resistance developed. In 1954 the Pan-American Sanitary Conference adopted a continental plan to eradicate malaria from the Americas. In 1955 this plan was extended to the world by the World Health Assembly (WHA). In 1956, the Sixth Expert Committee formulated a strategy for eradicating malaria (WHO 1957).

Soon after the WHA resolution and the report of the Expert Committee, most countries of the Americas, Europe, North Africa, Asia, and the Pacific officially declared that their antimalaria programs were eradication campaigns. In retrospect we can see that many of these programs were short on epidemiological knowledge and administrative capacity. These deficiencies were overlooked because of the programs' humanitarian appeal, the sense of urgency, and the feeling, shared by many, that peer pressure could shake the chronic apathy of the health services.

As anticipated, tropical Africa and some parts of Southeast Asia posed problems, because of their high endemicity, primitive state of development, and lack of human and economic resources. Successes elsewhere, although slower than expected, were still remarkable. But as more and more areas advanced into their program's consolidation phase, the expectation that a surveillance mechanism would maintain areas malaria-free, after spraying was interrupted, was not fulfilled. Resurgences occurred increasingly often in the consolidation and maintenance phase, particularly in Central America and Southeast Asia. And at the end of the decade a massive epidemic broke out in Sri Lanka, where malaria had been almost eradicated. Evidence began to accumulate that, although it was possible to reduce and even interrupt malaria transmission by spraying insecticide in large areas, it was difficult if not impossible to establish effective surveillance without a solid health infrastructure.

Finally, in 1969, after reexamining the global strategy of eradicating malaria, the World Health Assembly reaffirmed that eradication was the ultimate goal but stated that, in regions where eradication was not yet feasible, control of malaria with the means available should be encouraged and may be a necessary and valid step toward that goal (WHO 1969).

Unfortunately, after fifteen years of strictly regimented antimalaria action, health authorities—even malariologists—were reluctant to introduce the necessary changes in the programs while the concept of malaria control, and an acceptable global strategy for it, remained undefined. The Expert Committee provided only sketchy guidance on how to transform an ineffective malaria eradication program into a control program, emphasizing that "the objectives in these areas would be to consolidate the gains so far achieved, to extend the programme to areas where protection would give maximum socioeconomic benefit and to protect high risk groups" (WHO 1974, p. 30). Unfortunately, in most countries it was thought that the only way to consolidate gains achieved was to maintain as many routine activities as could be afforded, without making the necessary investment to evaluate their local effectiveness.

The formulation by WHO in 1978 of a strategy to develop a health care infrastructure included malaria control among its essential elements (WHO/UNICEF 1978). In line with these developments, the thirty-first World Health Assembly adopted a strategy of malaria control aimed at least at reducing mortal-

ity and the negative social and economic effects of the disease, preventing or controlling epidemics, and protecting malaria-free areas, with the ultimate objective of eradicating the disease whenever feasible (WHO 1978).

### *Malaria Control Measures*

The most common antimalarial measures are (a) chemical control through residual intradomiciliary spraying with DDT or other insecticides and, in selected instances, aerial spraying or local fogging, (ultra low volume); and (b) the treatment of fever cases with antimalarials. These activities are sometimes supported by limited environmental management measures mostly in urban areas where such measures can be easier to implement than in rural ones. They involve drainage or filling of water bodies. Water-level fluctuations or intermittent irrigation are used in some large development schemes. For all practical purposes biological control measures are presently of little relevance. In addition to these active intervention measures, all control programs undertake active or passive malaria surveillance. Specific antimalarial measures can be classified according to their mode of action and the scope and scale of their use (table 13-1).

Two substantially different approaches may be pursued in malaria control.

- Improving general health services to ensure adequate diagnosis, access to health care, and treatment for individual malaria cases, as well as promoting personal and community protection. The aim of this approach is to eliminate deaths from malaria and to reduce the severity and duration of illness associated with it.
- Establishing the capability for long-term control of malaria transmission, control and prevention of epidemics, and progressive reduction of malaria endemicity (particularly in areas affected by *P. falciparum*).

The two approaches are in no way mutually exclusive, and ideally they should be complementary; however, they differ greatly in their requirements for specialized services. Whereas the former is a basic requirement in all malarious areas, the second would be developed progressively, according to the intensity of the problem and resources available.

### *New Perspectives for Control*

In 1985 the thirty-eighth World Health Assembly expressed its continuing concern about resurgent malaria and, in particular, about the apparent inadequacies of existing malaria control strategies. Consequently, the WHO Expert Committee on Malaria (WHO 1986) reviewed the global malaria situation and attempted to develop further the epidemiological approach to malaria control, which had been proposed by the Expert Committee in 1979, giving particular emphasis to socioeconomic factors. Within the epidemiological approach is the recognition that variability among diverse malaria situations is the result of a multitude of factors, which will also affect the effectiveness of control measures. Mapping the distribution of these determining factors would constitute a "stratification" of the local malaria problem and would provide a useful framework for selecting and testing appropriate sets of control interventions.

### *Identification of Malaria Patterns*

In practice, the identification of all relevant epidemiological factors has not come easily to control program managers. They are often not equipped to analyze and interpret the massive quantities of epidemiological, parasitological, and entomological information that need to be collected—and to use this information to define appropriate control actions. In particular, those in charge of control programs have generally lacked the ability to see specific malaria situations in their economic and social context; that is, to analyze the relationships between patterns of human occupation and exploitation of the environment and trends in malaria transmission.

Nevertheless, accumulated experience and some specific studies of problem areas showed that there are identifiable ecological and social situations in which malaria is not only more frequent and serious but also more difficult to control. In the Brazilian Amazon, for example, economic, social, environ-

**Table 13-1. Malaria Control Measures**

| *Action* | *Individual and family protection* | *Community protection* |
|---|---|---|
| Reduction of man-mosquito contact | Bednets, repellents, protective clothing, screening of houses | Site selection, zooprophylaxis |
| Destruction of adult mosquitoes | Use of domestic space spraying | Residual indoor insecticides, space spraying, ultra-low volume sprays |
| Destruction of mosquito larvae | Peridomestic sanitation, intermittent drying of water containers | Larvicide for water surfaces, intermittent irrigation, sluicing, biological control |
| Source reduction | Peridomestic sanitation, small-scale drainage | Environmental sanitation, water management, drainage |
| Destruction of malaria parasites | Early diagnosis and treatment, chemoprophylaxis | Establishment of diagnosis and treatment facilities, chemoprophylaxis for pregnant women, mass treatment |
| Social participation | Motivation | Health education, community participation |

*Source:* Adapted from Bruce-Chwatt 1985.

mental, and political factors have converged to produce three epidemiological patterns, collectively referred to as "frontier malaria" (Marques 1988; Sawyer and Sawyer 1987; Wilson and Alicbusan-Schwab 1991). These patterns are found in the now famous "garimpos" (gold-mining areas), in areas of new agricultural settlement, and in the rapidly expanding periurban areas of the region. Although found in less than one in ten municipalities, they account for more than 80 percent of all malaria cases reported. Similarly, most malaria situations throughout the world, when viewed in their social and economic context, fall into a few main types.

It has been suggested (Nájera 1981, 1989) that it is possible to recognize and describe a limited number of prototypes or typical patterns, synthesizing, from a global perspective, those observations in different countries, complemented with summaries of control experiences in such situations. These descriptions of epidemiological patterns (which have been referred to as "prototyes" or "malaria paradigms") could help health planners in the important task of designing and implementing appropriate sets of control measures, either to develop new programs or to adapt existing ones.

### *Malaria Patterns and Specific Ecological Conditions*

The main determinants of malaria transmission (vector density and survival, human-vector contact and duration of parasite development in the vector) are dependent on availability of surface water and climate, which in turn have also influenced the distribution of rural populations and their agricultural activities. It is therefore possible to identify major differences in the epidemiology of malaria associated to the main types of ecological areas, which would provide a first characterization of the epidemiological pattern, unless man has sufficiently disturbed the environment and introduced some of the patterns referred to in the next heading.

THE AFRICAN SAVANNA. *Characteristics*: the African savanna represents the highest malaria endemicity in the world. The factors responsible for high levels of continuous transmission include propitious climatic conditions for vector breeding and the presence of such highly efficient vectors as *A. gambiae* and *A. funestus*. This pattern is characterized by high frequency of illness among young children and pregnant women, high childhood mortality, and high frequency of asymptomatic infections in older children and adults. Transmission may become seasonal in areas with less rainfall and at higher altitudes. Recently, the malaria problem has been aggravated by the rapid spread of drug resistance across the African continent.

*Control*: in the African savanna the most important goal of malaria control is to reduce the effect of the disease by providing effective treatment to all people suffering from malaria, which will require extension of services and health education to improve their use by the population. Pilot projects, aimed at the interruption of transmission in savanna areas, have been only partially successful, and institutional problems have constrained expansion of vector control programs (Bruce-Chwatt 1979 and Bruce-Chwatt and Archibald 1959 [Sokoto]; Foll and others 1965 and Nájera and others 1973 [Kankiya]; and Wilson 1960 [Pare Taveta]). There are some areas or population groups, however, in which vector control may be feasible; in particular it may be possible to introduce effectively insecticide-impregnated bed nets or curtains.

PLAINS AND VALLEYS OUTSIDE AFRICA. *Characteristics*: these areas correspond to the classic descriptions of malaria as a rural disease, being more intense in the poorest areas and in periods of economic depression. As in the African savanna, transmission may be from continuous to seasonal, depending on latitude, altitude, and aridity. The risk of transmission tends to increase with the introduction or extension of irrigation, but it considerably decreases with good water management and the improvement of farming techniques, houses, and animal shelters. In most of these areas malaria was brought under control by the early eradication campaigns, and vector control has continued over the last three decades. These areas show low endemicity and should continue to do so unless disturbed by civil unrest, insurgence, or war, which would not permit the functioning of health services.

*Control*: in most instances, it will be possible to maintain this favorable situation through the continuing development of their health and epidemiological services and by their ability to detect and control potential risk situations.

FOREST AND FOREST FRINGE AREAS. *Characteristics*: the extensive forest areas of Africa, South America, and Southeast Asia have increased in importance as the exploitation of forest resources has intensified. Malaria risks are associated with the type of human activity which modifies the microenvironment and the relation of humans and vectors to it. Nomadic and seminomadic tribal populations of forest areas, engaged in gathering and hunting, are generally too dispersed and mobile to sustain intense transmission. In the fringe of the forest or deforested areas, sedentary populations tend to be engaged mainly in agriculture, but they also use the forest to collect firewood and for hunting. In Africa the main malaria vectors, *A. gambiae* and *A. funestus*, follow man into the forest and, although they are more easily controlled than in the savanna, they are able to maintain the same levels of very high endemicity. In Asia and the Americas, settled population groups, engaged in regular agricultural activities in deforested areas, have a different malaria experience from that of those engaged in forest activities. The former suffer mostly from *P. vivax* infection and tend to have much lower malaria incidence, easily controllable with residual insecticides. In contrast, those engaging in activities at the edge of or inside the forest have a high risk of acquiring *P. falciparum* malaria.

*Control*: residual insecticides are practically ineffective against the highly exophylic (outdoor biters) forest vectors. Protection has been traditionally dependent on the use of drugs, often excessive and irregular, because of the absence of organized curative services. When international borders run across these areas, as is common in South America and South-

east Asia, there may be a concentration of illegal activities, which make areas even less accessible to programmed control. Chloroquine-resistant *P. falciparum* originated in areas of this type, both in the Colombian-Venezuelan and the Thai-Cambodian borders (Field 1967). Today more effective means of personal protection, such as pyrethroid-impregnated bed nets and repellents, offer a possibility of complementing the partial effect of currently available antimalarial drugs and eventually reducing the dependence on chemoprophylaxis.

HIGHLAND FRINGE AND DESERT FRINGE. *Characteristics*: altitude, drainage, and temperature are limiting factors in both mosquito breeding and in parasite development in the mosquito. Therefore, these factors have an important effect on the potential for malaria transmission along the fringes of highland areas. The highlands themselves, which tend to have less transmission of malaria, often are characterized by high population density and pendular migration between the highlands and neighboring valleys. These neighboring areas, which offer economic opportunities on plantations or in other development projects, often have more transmission. Unusually warm rainy seasons may cause serious epidemics in highland areas of low endemicity, resulting in high mortality (for example, East Africa and Madagascar in 1987–90). In Southeast Asia, vectors which breed in foothill streams (for example, *A. minimus* and *A. fluviatilis*) are more efficient vectors than those in the plains. Therefore, the foothills in such areas tend to be more malarious than the plains. In transitional zones adjoining deserts, the lengthy dry season also limits vector proliferation and malaria. Also, the populations of such areas tend to be dispersed and nomadic; epidemics may occur in years of exceptional rainfall or with the introduction of irrigation.

*Control*: as everywhere, effective disease treatment is fundamental in both highland and desert fringe areas. In addition, surveillance for the monitoring of epidemic risk indicators, and for the early detection of epidemics, is crucial. In different areas, different responses may be feasible. These responses may include a combination of preventive vector control, strengthening of treatment facilities, and mass fever treatment.

SEASHORE AND COASTAL MALARIA. *Characteristics*: the most typical situation is found where the mosquito vector breeds in brackish waters. Such mosquitoes are generally less efficient as vectors than those of neighboring inland areas, as is true of *A. melas* and *A. merus* in Africa and *A. aquasalis* in South America. Still, in Southeast Asia and the Pacific, *A. sundaicus* and *A. farauti* are responsible for serious malaria transmission. In some coastal areas, as in Central America and Mexico, freshwater-breeding mosquitoes may cause intense seasonal transmission by breeding profusely in estuaries closed during the dry season by a sand bar.

A frequent form of economic development in coastal areas is the establishment of tourist resorts, which often make important investments, not only in malaria control, but also in pest mosquito control, for the protection of the installations. The development of tourism often attracts more people than those that can make a living from the existence of the tourist resort, creating situations similar to those of periurban slums.

*Control*: disease control in tourist resorts is similar to that in urban areas. For rural coastal populations, whether they are engaged in agriculture or fishery, the basic measure should be case management and engineering methods, such as opening or flushing estuaries, land reclamation for agriculture or tree plantation, regulation of water courses, and so on.

URBAN MALARIA. *Characteristics*: except for some cities in southern Asia, where *A. stephensi* is fully adapted to the urban environment, malaria transmission does not occur in well-established, densely populated urban areas. Nevertheless, many tropical cities are surrounded by rapidly growing slums, which are basically a high concentration of shelters in what is still primarily a rural environment. Such situations increase the risk of malaria transmission. Eventually a high contamination of surface waters may prevent anopheline breeding before urbanization reaches the slum areas. Malaria transmission in urban areas varies considerably in space and time, but in certain situations it may be very high.

*Control*: malaria control in urban areas relies on environmental sanitation, in order to eliminate existing mosquito-breeding sites and prevent the creation of new ones. In addition, human-vector contact can be reduced through improved house construction and personal protection.

### *Malaria Patterns Associated with Specific Occupations or Social Conditions*

There are a number of socioeconomic activities which create major disturbances of the environment, attract large numbers of temporary workers, or disrupt the social structure and therefore the health care system. All these activities transform the basic epidemiological parameters, as determined by the physical ecology of the area. The new malaria patterns so created may be not very extensive in area or may not persist very long in the same location, but where and when they occur, they may represent authentic epidemiological explosions and often leave marked sequelae of environmental degradation when they are abandoned.

AGRICULTURAL COLONIZATION OF JUNGLE AREAS. *Characteristics*: areas of new colonization attract displaced people either from cities or from densely populated areas that often have low malaria endemicity. Many people have, therefore, no or little acquired immunity and suffer severely from malaria when exposed to the high-transmission risk in the jungle environment. The effectiveness of vector control based on intradomiciliary spraying is limited in these areas because shelters are generally precarious and the vector does not always feed or rest indoors. Social services in these areas are weak or absent. In time, the situation tends to improve as these settlements become more developed. This pattern is found in Brazil, parts of India, and the outer islands of Indonesia (Binol 1983; Marques 1988). The agricultural settlement of large new areas

is usually accompanied by the rapid growth of supporting urban centers as well. These centers attract large numbers of poor, often unemployed or underemployed migrants, who settle in precarious conditions on the urban periphery. This explosive periurban growth is also associated with high levels of malaria transmission (Sawyer 1986; Sawyer and Sawyer 1987).

*Control:* traditionally, protection has been dependent on the use of drugs, especially during the initial phases of settlement. The use of drugs, however, has often been excessive and irregular because of the absence of health services in these remote areas. Residual insecticides have proven less effective against highly exophylic forest vectors. In some areas traditional vector control activities may be possible. Furthermore, measures for personal protection, such as pyrethroid-impregnated bed nets and repellents, may be introduced in combination with appropriate information and health education.

GOLD AND GEM MINING. *Characteristics:* malaria is usually serious in remote forest areas among populations of miners who migrate frequently between existing mining areas, new mining areas, and urban and rural areas (for example, in Brazil and Venezuela). Occupation of these areas is often temporary, and investment in basic infrastructure and services is rare, especially in countries in which small-scale mining is illegal. *P. falciparum* drug resistance is frequent (for example, the Thai-Cambodian border, the Colombia-Venezuela border, and the Brazilian Amazon). Because they have tended to penetrate deeply into frontier areas, these gold and gem miners have often exposed highly vulnerable indigenous peoples to malaria and other diseases, with disastrous consequences.

*Control:* in these areas malaria control activities are exceedingly difficult. Case management is clearly a priority. Recently, attempts have been made to introduce insecticide-impregnated curtains and bed nets. In high-risk areas lacking any health facilities, it may sometimes be appropriate to establish specialized malaria clinics.

MIGRANT AGRICULTURAL LABOR. *Characteristics:* cotton, sugar, and large-scale rice cultivation often require large contingents of temporary labor for planting and harvesting. The workers generally live in crowded, unsanitary camps where mosquitoes abound and precarious shelters offer little protection against the malaria vector. Because of heavy pesticide use for agriculture, often sprayed by airplanes (especially in cotton farming), vector resistance to a broad spectrum of insecticides is common.

*Control:* disease control requires case management and the application of residual pesticides, where possible, and in some cases aerial pesticide application is very effective. In addition, personal protection measures, such as the use of insecticide-impregnated bed nets, can sometimes be applied. If irrigation practices allow, drainage, biological control, and other measures to reduce vector breeding may be indicated.

DISPLACED POPULATIONS. *Characteristics:* sociopolitical disturbances (such as wars, unrest, famines) often create situations in which the civilian population suffers a lack of basic supplies, destruction of houses, and considerable displacements, and even temporary or permanent housing in refugee camps. These situations, combined with the disruption of health services, may cause epidemic outbreaks even in areas previously well under control. These outbreaks particularly affect the civilian population; the military and police contingents are likely to benefit from organized control in their camps and chemoprophylaxis while in action.

*Control:* in these situations control depends on the size and organization of the refugee population and the intensity of the problem. It may be possible to consider mass fever treatment, temporary chemoprophylaxis, and even spraying of shelters. Sometimes relocation of camps and some sanitation measures are possible.

### *Patterns and Measures for Control*

The matrix in table 13-2 relates the patterns identified above with control measures that have or have not proven effective in malaria control programs. This table is neither comprehensive nor prescriptive; its intent is to help operationalize the concept of epidemiological stratification.

It must be noted that the diagnosis and treatment of cases, including the management of drug resistance, applies equally to all patterns. Case management and drug treatment, which in most cases represents the care of fever, without specific diagnosis, are dependent on the structure of the general health care system. Diagnosis and treatment should be undertaken by the general health services; in areas in which such services are weak or nonexistent, such as in forest fringe areas and frontier areas, special fever-treatment posts or malaria clinics may be needed. Transmission control interventions should be used selectively wherever they are affordable and can achieve sustainable results.

Vector control operations have relied overwhelmingly on spraying of residual insecticides. The effectiveness of residual spraying varies substantially with the biting and resting behavior of the mosquito vector, the type of housing, and the habits of the people. A control measure which is receiving increasing attention is the use of insecticide-impregnated bed nets or curtains.

Other techniques of vector control play a more restricted role but, where indicated, may be highly effective. Space or aerial spraying is seldom used and is rarely justified. Larvicides are feasible only with easily identifiable breeding places. Techniques of source reduction, such as drainage and water management, can be the measures of choice in urban and periurban areas and economic development projects. They are normally too costly, however, for widespread use.

### *Residual Practices from Malaria Eradication Programs*

Many malaria control programs continue to depend on practices held over from the eradication era that require adjustment. Indoor spraying of residual insecticides, the main

**Table 13-2. Patterns Associated with Ecological and Social Conditions**

| Control intervention | Major ecological conditions | | | | | | | Specific occupations/ social conditions | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | African savannah | Plains and valleys outside frica | Forest and forest fringe | Highland and desert fringe | Seashore and coastal | Urban | Agricultural colonization of forest | Gold mining | Migrant agri-culture labor | Displaced popula-tions |
| *Management of clinical malaria* | | | | | | | | | | |
| Diagnosis and treatment | + | + | + | + | + | + | + | + | + | + |
| Care of treatment failures | + | + | + | + | + | + | + | + | + | + |
| *Protection of pregnant women* | | | | | | | | | | |
| Chemoprophylaxis | + | – | + | – | – | – | + | – | – | – |
| Bednets and personal protection | + | + | + | + | + | + | + | + | + | + |
| *Vector control* | | | | | | | | | | |
| Residual spraying | – | Selective | Selective | Epidemic control | Selective | Limited | Selective | – | Limited | Epidemic control |
| Fogging ULV | – | – | – | – | + | Limited | – | – | Limited | + |
| Impregnated bednets or curtains | + | + | + | – | + | – | + | + | – | – |
| *Environmental control* | | | | | | | | | | |
| Drainage and source reduction | – | – | – | – | + | + | – | – | + | – |
| Larviciding | – | – | – | – | + | + | – | – | + | – |
| Biological control | – | – | – | – | Limited | + | – | – | + | – |
| *Surveillance* | | | | | | | | | | |
| Epidemiological surveillance | + | + | + | + | + | + | + | + | + | + |
| Monitoring epidemic risk | – | + | + | + | – | – | – | + | + | + |
| Health education | + | + | + | + | + | + | + | – | – | – |

*Source:* Authors.

control activity of eradication programs, consumes a large part of present program budgets. In principle, coverage with residual insecticides should be complete and regular to achieve significant reduction or interruption of transmission. Today's spraying is seldom regular because most budgets do not provide enough insecticide to cover all cycles; they are rarely complete because people often refuse to allow continuous routine spraying. Therefore, more selective, targeted, and cost-effective use of pesticides is needed.

Many malaria control programs continue the practice of case detection as the main mechanism to diagnose and treat malaria. This procedure, devised for the confirmation of the disappearance of malaria during the consolidation phase of a malaria eradication program, aims at the collection of a blood slide from every fever case in the population by a system of periodic house visits and the collaboration of all outpatient clinics of the health services. All fever cases are also given a single dose (presumptive) treatment to be followed by a full (radical) treatment, if the blood slide is positive, when the result from the laboratory becomes available, normally weeks or months later.

The consequence of insisting on a thick blood film for every fever case is that malaria microscopists are overwhelmed with negative slides, the examination of which not only takes most of their time but could also distract them and cause them to miss positives. The diagnosis is, most often, late, so it cannot help in the diagnosis of the cause of fever, and the radical treatment of positives, when offered, may no longer be needed. Reports to WHO indicate that 150 million slides are collected each year, with an average positive result of 3 to 5 percent. Great efforts are made in some malaria programs to maintain a network of laboratories staffed by reasonably trained microscopists, engaged most of the time in the diagnosis of ambulatory fevers. But those in charge of the programs do not feel responsible for making competent microscopy available in the medical care establishments for the diagnosis and monitoring of treatment of suspected severe malaria cases; case detection continues to serve mainly an epidemiological purpose and does not contribute to improve the quality of care delivered by the health services.

The epidemiological services of the malaria programs were designed to confirm that malaria had been eradicated, and were organized to achieve the direct confirmation that the parasite reservoir had been eliminated. Indirect indicators of risk were overlooked. As a result, malaria programs have a poor record for early detection, let alone the prediction, of malaria epidemics. Whereas poorly organized general health services, reporting abnormal increases of fever cases, detected a number of epidemics reported in the literature, the malaria program case-detection mechanisms operating in the area detected no abnormality until months later, when slides had been examined, the results reported, and the reported cases consolidated

and analyzed at the center. Often these mechanisms are unable to detect abnormal situations before they become large enough to overcome the dilution effect of consolidated reporting, as practiced by centralized malaria programs. General health services and local authorities are more sensitive and more likely to demand action in response to peripheral complaints, if encouraged to do so.

### *Interventions: Patterns, Cost-Effectiveness, and Choice*

The nature of the different scenarios has a strong effect on the choice of appropriate policies to combat malaria. Calculations of cost-effectiveness need to be made in each specific circumstance. The value of calculating cost-effectiveness of interventions is to help policymakers make decisions about competing uses of resources. The steps in any such analysis are the following: (a) identify the policy instrument which is actually under the control of the decisionmaker; (b) determine the relation between the policy instrument and the measure of outcome desired; (c) pursue the activity until the marginal effectiveness per unit of marginal cost falls to a level comparable to other uses of funds. Each of these components is problematic and each is sensitively related to the epidemiological pattern in which decisionmakers find themselves.

INTERVENTIONS. Often, the set of available policy options is clear. Still, there is sometimes confusion about what is actually controlled by the government. For example, chemoprophylaxis for pregnant women and insecticide-impregnated bed nets are included as control interventions. These are policies which promote the use of techniques of control, such as information, education, and communication activities (IEC) for prenatal care (in conjunction with a protocol for drug prescriptions); a subsidy on the sale of bed nets; active distribution of (free) materials; and an IEC campaign on appropriate use. Strictly speaking it is these latter policies which should be evaluated on the basis of costs and effectiveness.

Organizational, political, and social factors implicit in some of the patterns define or impose limits on the appropriate policies. For example, the policies involved with management of clinical malaria are specific to the structure of the general health care system. Costs associated with malaria are sensitive to the organization of the health system. Mills (1987) compares the costs of provision in vertical programs with those in integrated programs in Nepal and finds that the higher the volume of cases, the more similar the costs of the two organizational policies will be. In areas where caseloads are low, integrated programs can have substantial cost savings, because personnel can switch to other health needs as appropriate.

One decision concerning provision of treatment (for all complaints, not just malaria) would be the density of location of health centers, or, more realistically, the location of new centers. The difficulty in separating care for malaria from care for anyone who presents with fever is sharply defined in this case. Although probably the most important factor in the care of malaria in endemic areas, such decisions cannot possibly be made with regard to malaria alone. To the extent that malaria generates a large proportion of visits to health centers, however, this could argue for shorter distances to clinics in new areas of agricultural development (in relation to more stable communities) because of the greater severity of the disease in these areas, even though the set of appropriate interventions is the same for the two settings. Again, this is part of a much larger problem. In general, the interventions involved with case management are not specific to malaria and include protocols for the public health facilities; the regulation, taxation, or subsidization of drugs and private health care providers; and recommendations on care for these providers. Benefits accrue to the system from any of these interventions, but attributing them to malaria is misleading.

RETURNS TO SCALE. Costs per measure of outcome (deaths averted, discounted healthy life years gained) vary substantially with the level of activity of the intervention. Certain features of intervention programs are relatively fixed and therefore independent of scale of operation (facilities, staff salaries in the short run), others are variable and proportional to outputs, and still others rise more than proportionately with output. Assessing the (marginal) cost per unit of outcome achieved needs to be assessed in each context. At a global level, Molineaux (1988) speculates that there may be "decreasing returns," because many early programs of malaria reduction were recognized as having strong effects, whereas recent efforts have been more disappointing.

PORTFOLIO OF INTERVENTIONS. For a number of alternative policy options in malaria control, there is good reason to expect diminishing returns to most single activities and, therefore, to expect effective policies to entail a package of instruments. The cost of vector control activities will rise with expansion as a result of decreasing densities of vectors and of people. Costs of case management operations will rise also with decreasing frequency of cases and the eventual need for either public information or IEC campaigns, which are costly. Barlow and Grobar (1986) suggest that the great uncertainty surrounding cost estimates argues that a combination of policies need to be used in parasitic-disease control programs. This is an analogy to financial management in which a "portfolio" of instruments should be used to reduce the risk of the entire program's resulting in failure. Here, we argue that for malaria, at least, a combination of policies would be desirable even with accurate information, because of diminishing returns from any one instrument.

VECTOR CONTROL. The cost-effectiveness of residual spraying varies substantially with the endemicity of the disease in the locale and with the degree of intensity of use. In regions of low to medium endemicity, where either the elimination of the disease or a substantial reduction in prevalence in humans as a result of reductions in vector capacity is possible, the effectiveness of vector control may be high. It may also have thresholds or regions of "increasing returns" near levels at which eradication is possible. Generally, however, there are good reasons to expect rising marginal costs associated with

increasing workers hired for spraying. With decreasing density of housing units and increased distance from facilities in urban or regional centers, costs per house protected will rise as more person-hours will be needed for more remote areas. Similarly, small regions with high densities of the vector will be cheap to reach, whereas expansion to wider areas will become costly. Within a region, the cost per house protected will rise as a result of decreasing chemical effectiveness on the vector pool. Refusal of populations to have their dwellings sprayed also make improvements on the margin more difficult.

Other techniques of vector control play a much more restricted role. Space or aerial spraying is seldom used, except for urban epidemics or to interrupt short transmission seasons, and is rarely justified on cost grounds. Larvicides are feasible only with easily identifiable breeding places and are thus of limited use. Other source reduction techniques such as drainage and land management techniques can have significant effects in mainly urban areas, planned human settlements, or economic development projects, but they cannot be a significant part of widespread control operations.

CLINICAL MANAGEMENT. The cost of chemotherapy depends on both the costs of treatment itself and the costs (both to the health care system and to the individual) of getting the patient to seek treatment. For self-diagnosis (for over-the-counter purchases of chloroquine) or for spontaneous presentation at a health care facility, these costs are generally quite modest, although they depend on the availability of drugs and distances to facilities. For a target population of malaria sufferers who do not seek help in either of these forms, expansion of chemotherapy requires the use of information campaigns designed to encourage people to seek timely care or active case-detection methods, which are usually very expensive.

As to the effectiveness of drug treatment, to date, the use of chloroquine has been a remarkably effective and cheap method of dealing with the disease. People have been able to obtain the drug easily, and much treatment has taken place outside the formal health care system. One consequence of this may well have been the speeding of the progress of chloroquine resistance, that is, that marginal costs of chloroquine had been higher and increasing all along. The spread of chloroquine-resistant malaria has changed the picture substantially. Not only do the drugs cost more, but they also require more professional supervision; and some of them run into more serious problems of compliance with drug regimens. At 1987 prices (for one adult course of drug treatment), with chloroquine, the costs are $0.23 per person; with sulfadiazine/pyrimethamine, $0.50; with mefloquine/sulfadoxim/pyrimethamine, $1.20; and with quinine and tetracycline, $3.00. Drug treatment is likely to continue to be the principal antimalaria weapon. The possibility of multiple resistance and the difficulty of extending suitable health care to more remote rural areas, however, are two reasons why the cost of malaria control will continue to increase, if it is based on the indiscriminate use of antimalarial drugs.

PERSONAL PROTECTION. To some degree, the government can rely on public information messages to increase people's use of protective measures or to influence their use of drugs. The protective measures include bed nets, perhaps impregnated with insecticides, and modification of evening activities and clothing. For bed nets, a subsidy on their sale is also a possibility. Although bed nets themselves have been shown to reduce disease, the prospects for increasing their use remain unknown. Some people (more educated or concerned) may be quite easy to reach, but increasing usage of these measures to any great extent is probably expensive. To the extent that behavior does change, however, it can increase the effectiveness of antivector campaigns.

More rational use of antimalarial drugs should help to slow the spread of resistance, which has been encouraged by excessive and inappropriate use. To the extent that behavior can be changed by public information campaigns, this effect can be ameliorated. What this might cost and how much it might be worth require research geared to helping operations.

COST ANALYSIS FOR DECISIONMAKING. Most countries with malarious regions have in place some institutions designed to address the problem. The activities which are undertaken by these institutions depend partly on the local needs but also on history, cultural acceptability, and political concerns. The most practical use of cost information is its ability to assist the managers of the local malaria public health facility to make better incremental decisions in environments where they are constrained. When specific activities are proposed for a specific area, costs can be gauged relatively easily, because changes in scale are not at issue. Incremental benefits can also be appraised with regard to the local epidemiology and institutional and administrative conditions. Costing exercises in these cases can greatly improve allocation divisions by managers. Good examples of this use is the work done by Kaewsonthi and Harding (1986) in Thailand and by Mills (1987) in Nepal. In these studies, comparisons between techniques of vector control and between vector control and therapy are made clearer by careful costing procedures at local levels, and practical recommendations for improvements are made. Mills, for example, was able to suggest a reduction in active case-detection methods and an increase in malaria clinics (or other treatment facilities), observing that either of these activities looked better than spraying.

## Estimate of Cost-Effectiveness

From data in the papers by Barlow and Grobar (1986) and Mills (1987), we calculated the costs per year of life saved and cost-benefit ratios for a variety of countries (tables 13-3 and 13-4). The most striking feature of these numbers is their variability. Indeed, the differences between the studies are so marked that it would be hard to make any generalizations about them at all. The costs per case prevented ranged from $2.10 to $259 (in 1987 dollars), and the cost-benefit ratios, from 2.4 to 146. The higher cost-benefit figures make malaria control seem of utmost importance. The lower figures bring it into competition with many other government programs as well as with many estimates of the marginal deadweight loss from tax

**Table 13-3. Cost-Effectiveness Ratios in Malaria Control**

| Source | Country | Method | Cost per case prevented (1987 dollars) | Cost per death averted (1987 dollars) | Cost per discounted DALY saved with various case-fatality rates | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | 2% | 1% | 0.5% | Observed |
| Barlow 1968 | Sri Lanka | Insecticide | — | 78 | — | — | — | 2.8 |
| Cohn 1973 | India | Insecticide | 2.10 | — | 3.6 | 7 | 14 | — |
| Gandahusada and others 1984 | Indonesia | Insecticide | 83–102 | — | 142–174 | 284–349 | 564–693 | — |
| Hedman and others 1979 | Liberia | Vector control and chemotherapy | 14 | — | 24 | 48 | 95 | — |
| Kaewsonthi and Harding 1984 | Thailand | Vector control and chemotherapy | 27–74 | — | 46–127 | 92–253 | 183–502 | — |
| Mills 1987 | Nepal | Vector control and chemotherapy | 1.30–172 | — | — | — | — | 2.8–255 |
| Molineaux and Gramiccia 1980 | Nigeria | Vector control and chemotherapy | 259 | — | 443 | 886 | 1,759 | — |
| Ortiz 1968 | Paraguay | Insecticides | 60 | — | 103 | 205 | 407 | — |
| Walsh and Warren 1979 | Developing countries | Vector control | — | 990 | — | — | — | 34 |

— Data not available
*Source:* Barlow and Grobar 1989; Mills 1987; authors' calculations.

collection (the systematic undervaluation of costs of government sources). Part of the explanation of the wide range of variation is not very illuminating. Differences in data quality, the assumptions used in the analyses (for example, the estimation of mortality avoided), the definition of the relevant costs, the length of time studied, the discount rate applied, and the coverage and purpose of the original intervention account for much of this variation. As one example, in the Garki Project study (Molineaux and Gramiccia 1980), which generated the figure of $259 per case averted per year, the costs of the extensive research and monitoring exercise which accompanied the intervention are included in the program costs. Similarly, some of the studies included administrative costs, whereas others used only the cost of materials. Some costs were calculated on the basis of small pilot projects (Gandahusada and others 1984) and others on the basis of national efforts (Barlow 1968).

The last four columns of table 13-3 contain calculations of the cost per discounted disability-adjusted life-year (DALY) saved for differing assumptions concerning the case-fatality rate for those cases in which the study does not explicitly present that value. The numbers are sensitive to this assumption, much more so than to any other parameter in the DALY calculation. Any attempt to calculate the cost per discounted DALY saved by the program requires locally relevant estimates of case-fatality rates.[1]

There are more important, systematic reasons, however, to expect average costs per unit of output to vary substantially between studies: (a) differences in the ecological, epidemiological, and social characteristics between areas; (b) wide variations over time within areas of the incidence and severity of malaria; (c) variations in the organizational structure of control programs; and (d) differences in the intensity of application of the interventions being appraised.

**Table 13-4. Cost-Benefit Ratios in Malaria Control**

| Source | Country | Method | Cost |
|---|---|---|---|
| Barlow 1968 | Sri Lanka | Insecticide | 146 |
| Griffit, Rampana, and Mashaal 1971 | Thailand | Chemoprophylaxis | 6.5 |
| Khan 1966 | Pakistan | Eradication program | 4.9 |
| Livandas and Athanassatos 1963 | Greece | Eradication program | 17.3 |
| Niazi 1969 | Iraq | Eradication program | 6.0 |
| Ortiz 1968 | Paraguay | Insecticides | 3.6 |
| San Pedro 1967 | Philippines | Eradication program | 2.4 |
| Democratic Republic of Sudan 1975 | Sudan | Control program | 4.6 |

*Source:* Barlow and Grobar 1986.

## Priorities

Our perception of malaria has been changing rapidly over the past decades. Malaria is not, as once was thought, evenly spread over the geographic areas in which it is prevalent. Instead, it is highly focal, primarily affecting the hardest areas to reach, and it is intimately linked to development efforts such as agricultural development, road building, fiscal incentives, and colonization projects. Furthermore, malaria, which once was easily treatable with chloroquine, has reemerged as a new disease called drug-resistant malaria. Drug-resistant malaria has been spreading, and serious problems in treatment are becoming more and more common. Finally, parasite distribution has not remained stable, but there is a general increase and a general shift from the more benign tertial malaria caused by *P. vivax* to the fatal tropical malaria caused by *P. falciparum*.

Taking into account the epidemiology of malaria at present, the prevalent trends in the past fifteen to twenty years, and the prevailing level of endemicity in Africa south of the Sahara, it is reasonable to believe that a considerable deterioration of the situation is to be expected before the end of this century, unless a more serious control effort is made. Even if vaccines, new drugs, or new insecticides are developed, in view of the time required for their final testing in the field, they are unlikely to have a significant effect on malaria in the 1990s. The most critical activities that could accelerate the progress in malaria control can be summarized as follows:

- In countries of Asia, the Americas, and North Africa, in which organized malaria control activities have been carried out for nearly three decades, the priority should be on reassessment of activities. Replanning of programs must be based on epidemiological analysis, and at the same time, necessary changes in the organization and administration of these programs must be implemented.
- In countries of Africa south of the Sahara, priority should be given to the extension of coverage of population by the health care system. At the same time, a nucleus of malaria specialists should be trained and selective control programs started. This should allow realistic planning and implementation of malaria control activities. The implementation of any control activity on a larger scale should be preceded by epidemiological field study that would contribute to the better understanding of the local epidemiology of malaria.

### *Human Resources Development*

At the beginning of the malaria eradication program a significant effort was made to train the personnel needed for the program, but, as programs became staffed and because malaria was expected to disappear soon, technical people and, especially, professionals in medical and biological sciences became progressively scarce. It has been said that the global malaria eradication program did not eradicate malaria but did eradicate malariologists. Moreover, training for eradication was definitely oriented toward the execution of the highly standardized program tasks and operations. The training of malariologists did not give them the epidemiological background needed to adapt to changing situations, to solve problems, to manage uncertainty, or to adapt or change control methods and strategies.

To meet current needs and achieve sustainable control, it is essential to create the manpower needed and to reorient human resources, not only to apply standard solutions to recognized problems, but also to identify and find a solution to future problems. In that way we may be able to avoid repeating the cycle described in 1927, in the Second Report of the Malaria Commission of the League of Nations: "The history of special antimalarial campaigns is chiefly a record of exaggerated expectations followed sooner or later by disappointment and abandonment of work."

National training programs should be supported and coordinated to ensure, through technical collaboration between countries, that all countries are able to do the following:

- Maintain a corps of adequately trained professionals with the necessary epidemiological expertise to understand the malaria problem and to adapt control strategies and programs to new situations.
- Train and orient general health services staff in the clinical management of malaria, recognition and treatment of severe and complicated malaria, monitoring of drug resistance, and collection and management of epidemiological information.
- Develop appropriate training methods for nonprofessional workers and community health workers so they can better manage fever and promote personal protection and an improved environment.
- Promote the development of curricula in schools of medicine and schools of public health to include new strategies of malaria control and to increase their ability to stay abreast of the latest information on the diagnosis and treatment of malaria.

The development of new or improved methods or materials for malaria control—in particular, antimalarial drugs and potential vaccines—should continue to receive the highest priority. This view, which is widely supported and, to an important extent, has shaped the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases' (TDR) research priorities, was recently reconfirmed by the National Academy of Sciences/Institute of Medicine report on malaria.

## Research

The most damaging effect of the malaria eradication years was probably the neglect of malaria research and malariology's lack of appeal as a career to young scientists and epidemiologists. In the words of McGregor (1982 p. 126), "throughout the

world support for further research into malaria, even that concerned with insecticides and chemotherapeutics, contracted swiftly. Worse still, the apparently imminent demise of a once important disease removed the necessity for training scientists in malariology. It took 10 more years and a war to halt this tragic trend." The reawakening of interest in malaria research showed a marked bias toward new technological developments through laboratory-based research, mostly in chemotherapy, immunology, genetics, and the genetic control of vectors and the possible use of mosquito pathogens.

In particular, since 1976 the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) has assumed a key role in coordinating and funding malaria research. It has made malaria its first priority and continues to provide technical drive toward development of new tools for control.

Actually, most available antimalaria interventions are far from ideal, not only in effectiveness but in their suitability for incorporation into long-term policies or the everyday practices of peoples and communities. Moreover, many of them have lost much of their original effectiveness because resistant strains of parasites or anophelines have developed. We must improve our understanding of the epidemiology of malaria and of problems such as parasite and vector resistance. We must improve the tools of epidemiological investigation so we can identify problems in the field, plan and evaluate potential solutions, and more effectively target interventions to problems. We must understand and monitor social and economic processes that may influence the epidemiology of malaria and facilitate or hamper the effectiveness of potential control measures. And we must come to understand how these processes may facilitate the incorporation of malaria control in developing a health infrastructure.

Funding for malaria control programs shrank when people began to recognize that malaria could not be eradicated, when the "basic health services" strategy in developing a health infrastructure did not succeed, and when no successful models developed for incorporating malaria control into the primary health care strategy. Malaria and general public health services exhibited a nearly universal reluctance to redefine their responsibilities toward the malaria problem.

Research may provide new and improved technologies needed to extend the feasibility of control, may provide epidemiological tools that improve efficiency of control, and may show better ways to combine interventions in more effective and efficient strategies. But it is also necessary that any new tool be validated in the field and field tested to determine its applicability in disease control. It is important that researchers try to find better ways to integrate new and old tools for control. It is important to use health systems research to find the best ways to incorporate new methods of control into the health infrastructure and deliver them to individuals and communities. And as part of the strategy of primary health care, we must test ways to control malaria through research and development.

Malaria control and malaria research have drifted apart over the years. While malaria control programs continued their fight using an established set of tools, research institutions moved off in search of new technological solutions, and both were under increasing financial constraints. Support for malaria research contracted during the eradication years (McGregor 1982), even for research on pesticides and drugs, but support has been revived. This renewed research effort, however, has shown a marked bias toward laboratory research and toward the development of new technologies in chemotherapy, immunology, genetics, the genetic control of vectors, and the potential use of mosquito pathogens.

In some parts of the world, control programs and research institutions have developed a curious rivalry: programs are almost defensively entrenched in the use of established methods, such as residual spraying, whereas researchers uncritically proclaim as alternatives what should be seen as complementary techniques. On the whole, researchers have undertaken projects that are of little relevance to ongoing control operations and the specific problems of control institutions. At the same time, control programs, which often collect massive amounts of valuable information, have lacked the capacity to select research priorities and carry out research projects.

Given the present status of malaria and malaria control programs, we recommend that priority be given to research in the following areas:

*Epidemiology*. Research is needed to improve our epidemiological tools and understanding and thereby improve our ability to identify problem areas and better target control interventions. In particular, we must understand and monitor social and economic processes that may influence the epidemiology of malaria and facilitate or hamper the effectiveness of potential control measures.

*Technology*. Research is needed to develop and field-test new control technologies and new combinations of old interventions in order to increase efficiency and cost-effectiveness of control programs.

*Organization and management*. Research is needed on the organization and management of control programs in order to develop more effective and efficient organizational structures and management processes.

*Health infrastructure*. Research is needed on health systems to examine the potential and means for effective participation of the general health services in malaria control, in particular in epidemiological surveillance, diagnosis and treatment, and community mobilization. Many countries have embarked on a process of decentralization of health services that could impart negatively on the effectiveness of vertical malaria control programs. These countries, in particular, will need to move cautiously and study carefully the alternatives for increasing the capacity of the general health services to assume new responsibilities in disease control.

## Notes

1. For purposes of presentation, the other parameters in the DALY calculation were assumed to be twenty-nine discounted years gained per death averted, eight days of illness, and a 10 percent quality-of-life adjustment for nonfatal cases. Except at very low case-fatality rates, the calculations are quite insensitive to large ranges in the assumed values of these three parameters.

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